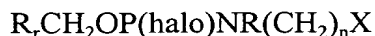


What is claimed is:

1. A compound of the formula



wherein

- 5 R is C<sub>1</sub>-C<sub>4</sub> alkyl or -(CH<sub>2</sub>)<sub>n</sub>X;

n is 4 or 5;

X is an electrophilic group capable of being nucleophilically displaced from its bonded carbon atom;

halo is chloro, bromo or iodo; and

- 10 the group R<sub>r</sub>CH<sub>2</sub>- is a biologically labile ester forming group.

2. The compound of claim 1 wherein n is 4.

3. The compound of claim 1 wherein n is 5.

4. The compound of claim 1 wherein R is methyl.

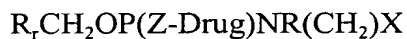
5. The compound of claim 1 wherein halo is chloro.

- 15 6. The compound of claim 1 wherein X is chloro or bromo.

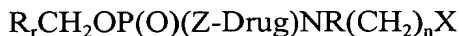
7. A method of preparing a phosphoramidate prodrug for enhanced intracellular delivery of a drug as phosphate ester or amide said method comprising the steps of reacting a hydroxy functional or amino functional drug compound (Drug-ZH) with a compound of the formula

- 20  $R_rCH_2OP(halo)NR(CH_2)_nX$

under conditions conducive to the formation of an intermediate compound of the formula



and oxidizing that intermediate to form the phosphoramidate prodrug of the formula



5

$n$  is 4 or 5;

halo is chloro, bromo or iodo; and

the group  $R_fCH_2-$  is a biologically labile ester forming group.

10

formula



$q$  and  $k$  are independently 1 or 0; and

B is H, amino, protected amino or C<sub>1</sub>-C<sub>4</sub> alkanoylamino.

20

11. A phosphoramidate compound formed from a hydroxy functional or amino functional drug compound of the general formula Drug-ZH said prodrug being a compound of the formula

R is C<sub>1</sub>-C<sub>4</sub> alkyl or -(CH<sub>2</sub>)<sub>n</sub>X;

Z is O or N;

halo is chloro, bromo or iodo; and

the group  $R_rCH_2-$  is a biologically labile ester forming group.

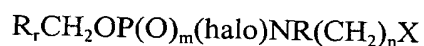
13. The method of claim 12 wherein Drug-ZH is a peptidomimetic of the formula



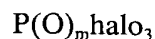
$q$  and  $k$  are independently 1 or 0; and

- 20 B is H, amino, protected amino or C<sub>1</sub>-C<sub>4</sub> alkanoylamino.

15. A method of preparing a compound of the formula



comprising the steps of reacting a compound of the formula



with 1) an alcohol of the formula  $R_rCH_2OH$  and 2) an amine of the formula

5  $HNR(CH_2)_nX$ , each in the presence of an acid scavenger,

wherein in the above formulas

m is 0 or 1;

R is  $C_1$ - $C_4$  alkyl or  $-(CH_2)_nX$ ;

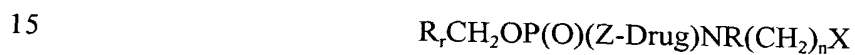
n is 4 or 5;

10 X is an electrophilic group capable of being nucleophilically displaced from its bonded carbon atom;

halo is chloro, bromo or iodo; and

the group  $R_rCH_2-$  is a biologically labile ester forming group.

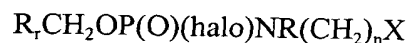
16. A method of preparing a phosphoramidate prodrug of the formula



for enhanced intracellular delivery of a compound of the general formula  $Drug-ZPO_3$

said method comprising the steps of reacting a hydroxy functional amino functional drug

compound of the formula  $Drug-ZH$  with a compound of the formula



20 under conditions conducive to the formation of the prodrug

wherein in the above formulas

R is  $C_1$ -C alkyl or  $-(CH_2)_nX$ ;

n is 4 or 5;

Z is O or N;

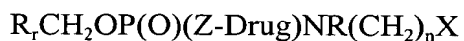
OR

X is an electrophilic group capable of being nucleophilically displaced from its bonded carbon atom;

halo is chloro, bromo or iodo; and

the group  $R_1CH_2-$  is a biologically labile ester forming group.

- 5            17. A pharmaceutical composition comprising  
a phosphoramidate compound formed from a hydroxy functional or amino functional drug compound of the general formula Drug-ZH said prodrug being a compound of the formula



- 10        wherein

R is  $C_1-C_4$  alkyl or  $-(CH_2)_nX$ ;

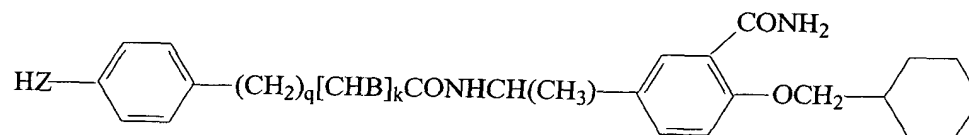
n is 4 or 5;

Z is O or N;

- 15        X is an electrophilic group capable of being nucleophilically displaced from its bonded carbon atom;  
halo is chloro, bromo or iodo;  
the group  $R_1CH_2-$  is a biologically labile ester forming group; and  
a pharmaceutically acceptable carrier therefor.

18.        The pharmaceutical compound of claim 17 wherein Drug-ZH is an amino  
20        acid or a biologically active peptide or peptidomimetic.

19.        The pharmaceutical composition of claim 18 wherein Drug-ZH is a peptidomimetic of the formula



5

wherein Z is O or N;

q and k are independently 1 or 0; and

B is H, amino, protected amino or C<sub>1</sub>-C<sub>4</sub> alkanoylamino.

20. The pharmaceutical composition of claim 17 wherein Drug-ZH is a nucleotide analog.

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